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Assessment of Renal Function in A Rural Population by Different GFR Estimation Methods

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Abstract: ***Background:*** Accurate measurement of renal function is critical for diagnosing and stratifying kidney disease. Various methods to estimate glomerular filtration rate (GFR) have shown variable results depending on the studied population. ***Objective:*** This study aimed to evaluate the effectiveness of different GFR estimation methods in assessing renal function in a selected rural adult population. ***Method:*** A cross-sectional study was conducted from July 2019 to June 2020, including 222 participants based on specific inclusion and exclusion criteria. Detailed histories and relevant investigations were obtained from each participant. Estimated GFR (eGFR) was calculated using serum creatinine, cystatin C, and combined formulas. Data were recorded in separate case record forms and analyzed using SPSS 26.0 and MedCalc 13.0. ***Results:*** The mean (±SD) age of the study population was 41.12±12.72 years, with a majority aged 31-50 years (59.5%). There was a male predominance (53.6%). Mean eGFRs were as follows: MDRD 117.31±25.54 mL/min/1.73 m², Cockcroft-Gault 102.87±30.50 mL/min/1.73 m², CKD-EPI 119.52±20.48 mL/min/1.73 m², cystatin C-based 107.17±16.34 mL/min/1.73 m², and combined creatinine-cystatin C 105.48±20.87 mL/min/1.73 m². Renal function assessment by MDRD, Cockcroft-Gault, CKD-EPI, cystatin C, and combined equations showed significant agreement with each other. ***Conclusions:*** Different GFR estimation methods showed no clear superiority over each other. However, eGFR CKD-EPICr demonstrated perfect agreement with the MDRD equation, and eGFR CKD-EPICys showed substantial agreement with eGFR CKD-EPICr-Cys.

Keywords: Renal function, GFR estimation, MDRD, CKD-EPI, Cystatin C.

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Article at a glance:

Study Purpose: *To evaluate renal function using different GFR estimation methods in a rural population.*

Key findings: *Good agreement among various GFR estimation methods, with eGFR CKD-EPICr perfectly aligning with MDRD and eGFR CKD-EPICys substantially agreeing with eGFR CKD-EPICr-Cys.*

Newer findings: *This study confirms the reliability of cystatin C-based equations alongside creatinine-based ones for assessing renal function, particularly in rural populations.*

Abbreviations: *AKI: Acute Kidney Injury, BP: Blood Pressure, CG:, Cockcroft-Gault, CKD: Chronic Kidney Disease, ERC:, Ethical Review Committee, ESRD: End Stage Renal Disease, GFR: Glomerular Filtration Rate, ICU: Intensive Care Unit.*

INTRODUCTION

Evaluating the glomerular filtration rate (GFR) is essential for assessing renal function, widely acknowledged as the best overall index of kidney health. Accurate GFR measurement is crucial for diagnosing, staging, and managing

chronic kidney disease (CKD).[1] GFR can be measured directly through the clearance of exogenous filtration markers, such as inulin and iohexol, or indirectly using endogenous markers.[2] The ideal marker for GFR estimation should be an endogenous molecule produced at a constant rate, cleared solely by the kidneys via free glomerular filtration, without secretion by tubular cells or reabsorption into peri-tubular circulation. The gold standard for determining GFR involves the clearance of exogenous substances like inulin, 51Cr-EDTA, iohexol, 125I-iothalamate, and 99mTc-DTPA, which are exclusively excreted through glomerular filtration. However, these techniques are time-consuming, labor-intensive, expensive, and require the administration of substances, making them impractical for routine clinical use.[3]

Commonly used endogenous markers for renal function include serum creatinine, urea, uric acid, and electrolytes. The effectiveness of additional markers, such as cystatin C and β-trace protein, has also been evaluated.[4] Serum creatinine (SCr) is the most widely used endogenous filtration marker in clinical practice. However, its concentration can be influenced by factors such as age, gender, race, body size, muscle mass, and food intake, potentially leading to overestimation in serum and underestimation in calculated clearance. Additionally, serum creatinine levels can appear normal in individuals with significantly impaired GFR, complicating real-time evaluation in unstable, critically ill patients.[5] Serum cystatin C, an alternative endogenous marker less affected by non-renal factors, has been suggested as an early marker for detecting changes in GFR and assessing renal impairment more accurately at an earlier stage than serum creatinine. Cystatin C is a single-chain, non-glycosylated basic protein produced by all nucleated cells at a constant rate. Its low molecular weight (13 kDa) and cationic nature ensure its free passage through the glomerulus. Unlike creatinine, cystatin C concentration is independent of muscle mass, gender, age, or nutritional status and is not affected by inflammation, fever, or other agents.[6] However, estimated GFR (eGFR) calculated using serum creatinine and/or cystatin C is widely used in clinical practice and epidemiologic research but lacks precision and accuracy when GFR is <60 mL/min/1.73 m².[7]

Several equations are popular for estimating GFR, including Cockcroft-Gault (CG), four-variable modified diet in renal disease (4v-MDRD), and chronic kidney disease epidemiology collaboration (CKD-EPI). Each has its limitations. The CG equation, derived from an inpatient population predominantly consisting of male CKD patients, does not correct for race and requires height and weight to adjust for body surface area (BSA). The MDRD equation, derived from a predominantly white population with kidney disease, offers a rapid method for assessing renal function but also relies on serum creatinine and demographic data. Both C&G and MDRD formulas have been used in individuals with known renal diseases and normal serum creatinine levels.[8,9] Given the high prevalence of kidney-related diseases and the necessity for accurate kidney function evaluation, it is essential to study the sensitivity and specificity of different GFR estimation methods. Therefore, this study aimed to assess renal function in a rural population using various GFR estimation methods.

OBJECTIVES

General

To see the pattern of GFR by different estimation equation in rural
population

Specific

To estimate the GFR by serum Creatinine
To estimate the GFR by plasma cystatin C
To Calculate the GFR by different equation-based formula
To observe any agreement between methods

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted from July 2019 to June 2020 at the Department of Nephrology, National Institute of Kidney Diseases and Urology. The study aimed to evaluate renal function using different GFR estimation methods in a rural population. A total of 222 participants, aged 18 years and older, were selected based on specific inclusion and exclusion criteria. Detailed histories and relevant investigations were performed for each participant. Blood samples were collected for serum creatinine and cystatin C measurements.

Inclusion Criteria

Adults aged 18 years and older
Residents of Baidyerbazar union, Sonargaon, Narayanganj, Bangladesh
Participants who provided informed written consent
Participants willing to undergo all required clinical and biochemical evaluations

Exclusion Criteria

Pregnant women
Patients currently undergoing treatment for cancers
Patients with cognitive impairment
Individuals unable to provide informed consent

Data Collection

Participants were randomly selected from the voter list of Baidyerbazar union, Sonargaon, Narayanganj. Detailed demographic, clinical, and biochemical information was collected through structured interviews and medical examinations. Blood samples were taken after overnight fasting for serum creatinine and cystatin C measurements. The samples were centrifuged, aliquoted, and stored at -80°C until analysis. Data were recorded in pre-designed case record forms. Clinical evaluations and blood sample collections were conducted at a local hospital, ensuring accessibility for the rural population.

Data Analysis

Data analysis was performed using SPSS version 26 and MedCalc 13.0. Quantitative data were expressed as means and standard deviations, while qualitative data were presented as frequencies and percentages. Agreement between different GFR estimation methods was evaluated using kappa statistics and Bland-Altman plots. The differences between continuous variables were assessed using Student's t-tests, and ANOVA was used to compare means among multiple groups. P-values <0.05 were considered statistically significant. Data were visualized in tables and graphs to present the results clearly and concisely, facilitating the comparison of various GFR estimation methods.

Ethical considerations

Informed written consent was obtained from all participants. The study's purpose and procedures were clearly explained, ensuring participants' understanding and voluntary involvement. Participants had the right to refuse or withdraw at any time without any consequences. Confidentiality was strictly maintained throughout the study. No physical or mental harm was posed to participants, and no financial incentives were provided. The study was approved by the ethical review board of the National Institute of Kidney Diseases and Urology.

RESULT

Table 1: Sociodemographic Profile of the Study Subjects (n=222)

Demographic Variables	Number of Patients	Percentage (%)
Age (years)		
18-30	46	20.7
31-40	67	30.2
41-50	65	29.3
51-60	25	11.3
>60	19	8.6
Mean age (years)	41.12±12.72	
Residence (Rural)	222	100.0
Educational Status		
No scholarship	10	4.5
Up to SSC	187	84.2
HSC	13	5.9
Graduation and above	12	5.4
Occupation		
Housewife	102	45.9
Service	26	11.7

Business	51	23.0
Student	8	3.6
Farmer	15	6.8
Unemployed	20	9.0
Marital Status		
Married	196	88.1
Unmarried	16	7.2
Divorced	3	1.4
Widow / Widower	7	3.1

The demographic profile reveals a predominance of participants aged 31-50 years (59.5%), with a mean age of 41.12±12.72 years. The entire study population resides in rural areas (100%), indicating a focus on a specific community. Educationally, 84.2% have studied up to SSC, while only 5.4% have completed graduation or higher, highlighting limited access to higher education. Occupation-wise, 45.9% are housewives, 23.0% are engaged in business, and 11.7% are in service roles, reflecting traditional gender roles and occupational distribution in rural settings. The majority are married (88.1%), 7.2% are unmarried, and 4.5% have other marital statuses, suggesting stable family structures. This demographic insight is crucial for understanding the socioeconomic factors influencing renal health and the applicability of GFR estimation methods in this specific rural population.

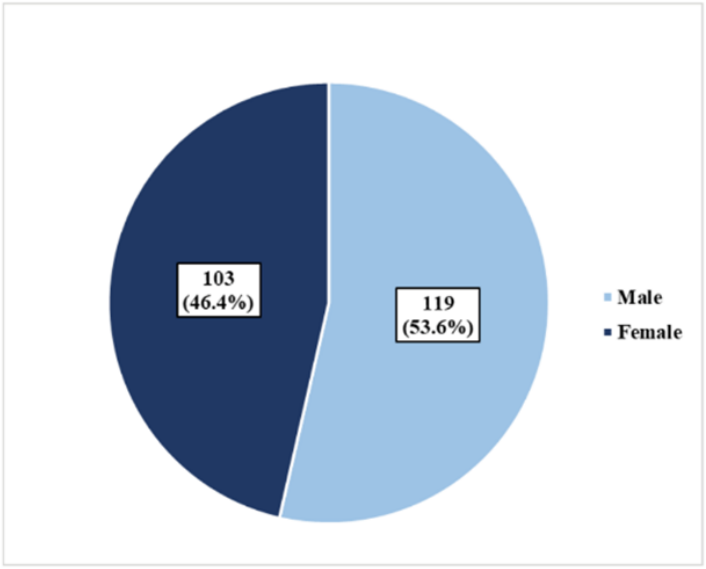

Figure 1: Distribution of Study Population According to Gender (n=222)

The study population comprised 119 males (53.6%) and 103 females (46.4%). This indicates a slight male predominance. Understanding gender distribution is essential for analyzing gender-specific health patterns and the effectiveness of renal function assessment methods across different demographic groups.

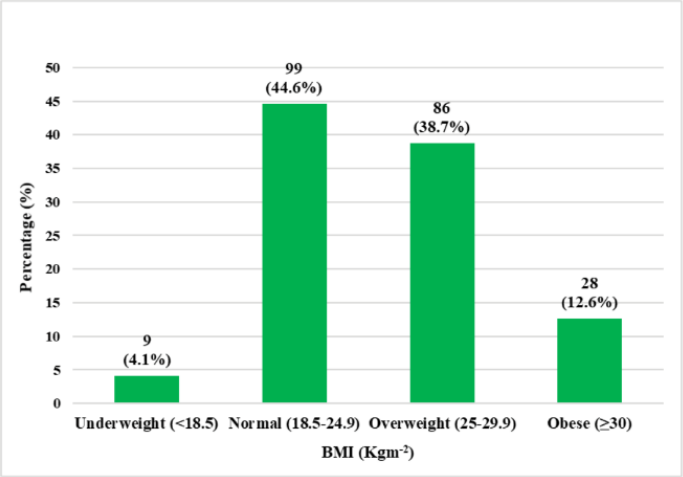

Figure 2: Subjects as per BMI (Body Mass Index) Category (n=222)

Among the 222 subjects, 44.6% had a normal BMI (18.5-24.9 kg/m²), 38.7% were overweight (25-29.9 kg/m²), 13.5% were obese (≥30 kg/m²), and 3.2% were underweight (<18.5 kg/m²). The mean BMI was 25.33±4.19 kg/m².

Table 2: Serum Creatinine and Plasma Cystatin C Values According to Gender (n=222)

Parameter	Mean (±SD)	Male	Female	P-value
Serum creatinine (mg/dL)	0.81±0.16	0.87±0.14	0.74±0.15	<0.001
Plasma Cystatin C (mg/L)	0.88±0.22	0.93±0.22	0.81±0.20	<0.001

The mean serum creatinine was 0.81±0.16 mg/dL, with males showing higher levels (0.87±0.14 mg/dL) compared to females (0.74±0.15 mg/dL) (p<0.001). Similarly, the mean plasma cystatin C was 0.88±0.22 mg/L, with males (0.93±0.22 mg/L) also higher than females (0.81±0.20 mg/L) (p<0.001). These significant differences highlight gender-specific variations in renal function markers.

Table 3: Measurement of Renal Function by Different Equations (n=222)

Equations	Mean (±SD)	Male	Female	P-value
MDRD (mL/min/1.73 m²)	117.31±25.54	123.33±26.47	110.36±22.62	<0.001
Cockcroft-Gault (mL/min/1.73 m²)	102.87±30.50	105.27±31.44	100.10±29.27	0.209
CKD-EPI (mL/min/1.73 m²)	119.52±20.48	122.02±19.10	116.63±21.71	0.050
CKD-EPI Cystatin C (mL/min/1.73 m²)	107.17±16.34	107.08±16.72	107.27±15.97	0.932
CKD-EPI Cr-Cys (mL/min/1.73 m²)	105.48±20.87	100.40±20.63	111.35±19.65	<0.001

The mean eGFR values using various equations showed significant gender differences. The MDRD equation indicated higher eGFR in males (123.33±26.47 mL/min/1.73 m²) than females (110.36±22.62 mL/min/1.73 m²) (p<0.001). CKD-EPI also showed higher eGFR in males (122.02±19.10 mL/min/1.73 m²) compared to females (116.63±21.71 mL/min/1.73 m²) (p=0.050). However, the Cockcroft-Gault and CKD-EPI Cystatin C equations did not show significant gender differences. CKD-EPI Cr-Cys revealed lower eGFR in males (100.40±20.63 mL/min/1.73 m²) than females (111.35±19.65 mL/min/1.73 m²) (p<0.001).

Table 4: Measurement of Renal Function by Different Equations (n=222)

Equation	eGFR (>90)	(%)	eGFR (60-90)	(%)	eGFR (<60)	(%)
MDRD	192	86.5	28	12.6	2	0.9
Cockcroft-Gault	151	68.0	49	22.1	22	9.9
CKD-EPI	197	88.7	23	10.4	2	0.9

CKD-EPI Cystatin C	195	87.8	27	12.2	-	-
CKD-EPI Cr-Cys	170	76.6	52	23.4	-	-

The majority of participants had eGFR values >90 mL/min/1.73 m² across all equations, with CKD-EPI showing the highest percentage (88.7%). Cockcroft-Gault had the lowest percentage in the >90 category (68.0%) and the highest in the <60 category (9.9%). This variation highlights differences in sensitivity and specificity among the equations.

Table 5: Measurement of Renal Function According to BMI Category by Different Equations (n=222)

Equation	Underweight	Normal	Overweight	Obese	P-value
eGFR MDRD (mL/min/1.73 m²)	111.0±20.7	119.4±28.8	116.8±24.1	113.7±18.3	0.622
eGFR Cockcroft-Gault (mL/min/1.73 m²)	66.5±16.9	92.4±28.5	110.7±25.9	127.5±28.1	<0.001
eGFR CKD-EPI (mL/min/1.73 m²)	114.2±19.2	120.1±22.7	119.6±18.9	118.8±17.7	0.868
eGFR CKD-EPI Cystatin C (mL/min/1.73 m²)	107.3±10.5	107.9±18.9	107.4±15.0	104.1±11.5	0.766
eGFR CKD-EPI Cr-Cys (mL/min/1.73 m²)	100.4±15.4	105.5±22.2	106.4±20.7	104.0±18.7	0.841

The MDRD equation showed stable eGFR values across BMI categories: underweight (111.0±20.7), normal (119.4±28.8), overweight (116.8±24.1), and obese (113.7±18.3), with a p-value of 0.622, indicating no significant variability. This suggests that MDRD is less influenced by BMI variations, making it a reliable equation for diverse populations. The Cockcroft-Gault equation exhibited significant variability: underweight (66.5±16.9), normal (92.4±28.5), overweight (110.7±25.9), and obese (127.5±28.1), with a p-value of <0.001. This equation's sensitivity to BMI is likely due to its incorporation of weight into the calculation, which significantly impacts the eGFR values. Thus, it requires careful interpretation in patients with extreme BMIs. The CKD-EPI equation displayed consistent eGFR values: underweight (114.2±19.2), normal (120.1±22.7), overweight (119.6±18.9), and obese (118.8±17.7), with a p-value of 0.868, indicating no significant differences. This equation's robustness across BMI categories supports its use in varied populations.

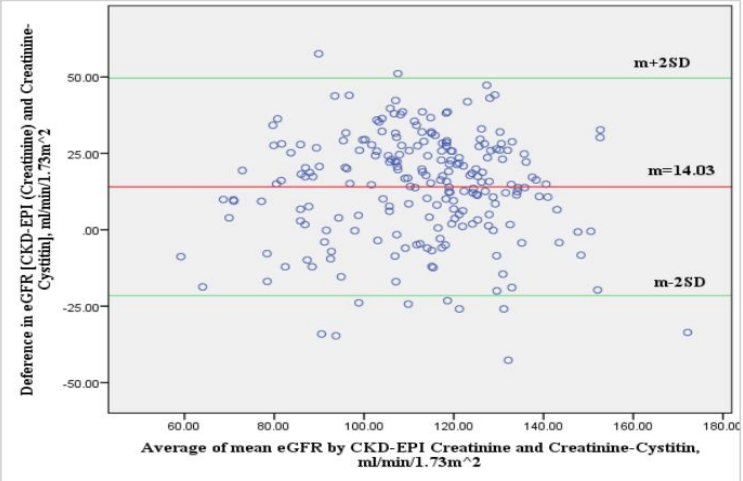

Figure 3: Comparisons of glomerular filtration rate estimated with eGFRCr and eGFRCys-Cr (Bland-Altman test) (n=222)

The CKD-EPI Cystatin C equation also showed minimal variability: underweight (107.3±10.5), normal (107.9±18.9), overweight (107.4±15.0), and obese (104.1±11.5), with a p-value of 0.766. Cystatin C is less influenced by muscle mass, making it a stable marker across different body compositions.

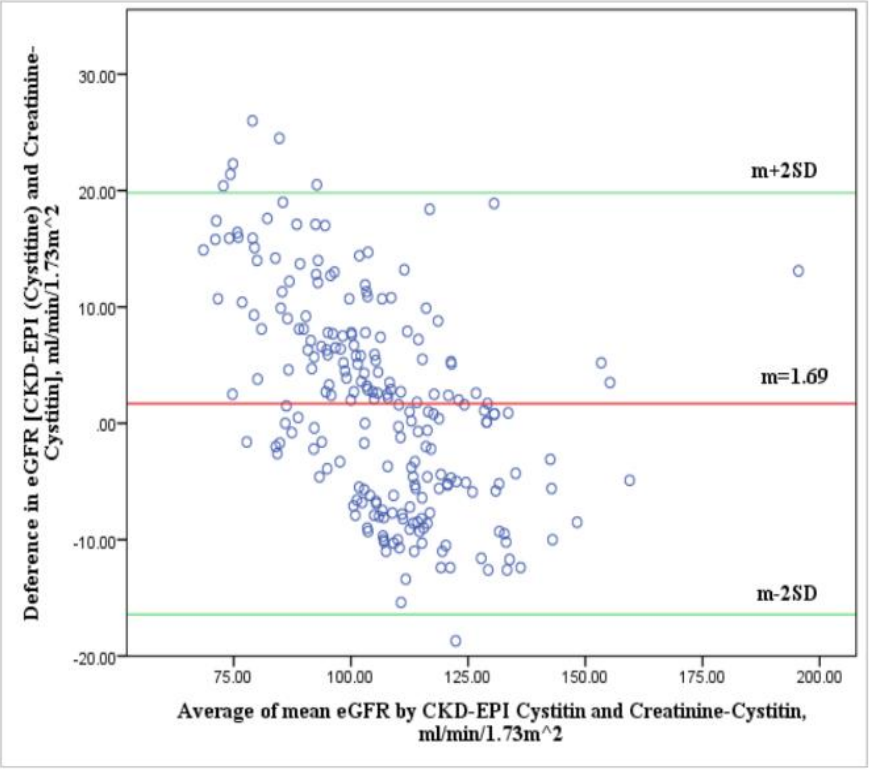

Figure 4: Comparisons of glomerular filtration rate estimated with eGFRCys and eGFRCys-Cr (Bland-Altman test) (n=222)

The combined CKD-EPI Cr-Cys equation showed slight variability: underweight (100.4±15.4), normal (105.5±22.2), overweight (106.4±20.7), and obese (104.0±18.7), with a p-value of 0.841. The combination of creatinine and cystatin C provides a balanced approach, enhancing accuracy.

Table 6: Agreement Between MDRD and Cockcroft-Gault (n=222)

Cockcroft-Gault	MDRD eGFR (>90)	MDRD eGFR (60-90)	MDRD eGFR (<60)	κ
eGFR (>90)	147	4	0	0.294
eGFR (60-90)	36	13	0	
eGFR (<60)	9	11	2	

The agreement between MDRD and Cockcroft-Gault equations showed fair agreement (κ=0.294). For MDRD eGFR (>90), 147 patients had eGFR >90 by Cockcroft-Gault, 4 had eGFR 60-90, and none had eGFR <60. This variability indicates moderate consistency between the two methods.

Table 7: Agreement Between MDRD and CKD-EPI (n=222)

CKD-EPI	MDRD eGFR (>90)	MDRD eGFR (60-90)	MDRD eGFR (<60)	κ
eGFR (>90)	191	6	0	0.856
eGFR (60-90)	1	22	0	
eGFR (<60)	0	0	2	

The agreement between MDRD and CKD-EPI equations showed almost perfect agreement (κ=0.856). For MDRD eGFR (>90), 191 patients had eGFR >90 by CKD-EPI, 6 had eGFR 60-90, and none had eGFR <60. This indicates high consistency between the two methods.

Table 8: Agreement Between CKD-EPI Cystatin C and CKD-EPI Cr-Cys (n=222)

CKD-EPI Cystatin C	CKD-EPI Cr-Cys eGFR (>90)	CKD-EPI Cr-Cys eGFR (60-90)	κ
seGFR (>90)	170	25	0.623
eGFR (60-90)	0	27	

The agreement between CKD-EPI Cystatin C and CKD-EPI Cr-Cys equations showed substantial agreement (κ=0.623). For CKD-EPI Cystatin C eGFR (>90), 170 patients had eGFR >90 by CKD-EPI Cr-Cys, and 25 had eGFR 60-90. This demonstrates a strong consistency between the two methods.

DISCUSSION

This cross-sectional study was carried out in a rural area of Sonargaon Upazilla, Bangladesh, involving 222 participants recruited purposively through a cardio-renal screening program.[10,11] The study aimed to assess renal function using serum creatinine, plasma cystatin C, and estimated GFR (eGFR) calculated by different equations based on serum creatinine and cystatin C. The mean (±SD) age of the participants was 41.12±12.72 years, with the majority (59.5%) aged between 31 and 50 years. All participants resided in rural areas, with 84.2% having education up to SSC level, and 53.6% were male. The primary diseases identified were diabetes mellitus (6.8%) and hypertension (11.3%). Our study found that the mean (±SD) serum creatinine was 0.81±0.16 mg/dL and plasma cystatin C was 0.88±0.22 mg/L, with significantly higher values among males compared to females. This aligns with findings from,who reported similar gender differences in serum creatinine levels.[12] The mean (±SD) eGFR measured by creatinine-based MDRD, Cockcroft-Gault (C&G), and CKD-EPI equations were 117.31±25.54, 102.87±30.50, and 119.52±20.48 mL/min/1.73 m², respectively. The mean (±SD) eGFR measured by cystatin C-based equation was 107.17±16.34 mL/min/1.73 m², and by using both creatinine and cystatin C, it was 105.48±20.87 mL/min/1.73 m².

Interestingly, our findings show that the mean eGFR values calculated by C&G and the combined creatinine and cystatin C equation were lower compared to other creatinine-based equations. This pattern of lower eGFR values with C&G has been observed in other studies as well, such as,which reported fair agreement between MDRD and C&G equations (κ = 0.294).[13] In contrast, serum creatinine-based CKD-EPI showed almost perfect agreement with the MDRD equation (κ = 0.856), and substantial agreement was observed between CKD-EPIcys and CKD-EPIcr-cys (κ = 0.623).

Comparison with Existing Literature

The distribution of eGFR values in our study (>90, 60-90, <60 mL/min/1.73 m²) was consistent with findings from other studies, such as those by,which showed similar age distributions and CKD prevalence among asymptomatic adult populations in Bangladesh.[14] However, the slightly higher mean age in the Zeba et al. study (48.94±11.00 years for control and 53.09±11.11 years for CKD patients) compared to our study (41.12±12.72 years) could be attributed to differences in the target population and study design. Many studies have compared cystatin C concentrations or cystatin C-derived equations with gold standard methods, finding cystatin C to be superior or at least equivalent to serum creatinine for detecting decreased GFR.[15] Our study supports these findings by demonstrating substantial agreement between cystatin C-based and creatinine-based equations. However, the slight differences in eGFR values across various studies could be attributed to variations in sample size, population demographics, and geographical factors. For instance, differences in muscle mass, dietary habits, and genetic factors among populations can influence serum creatinine and cystatin C levels, as suggested by.[16]

Practical Implications and Recommendations

Our findings highlight the importance of using multiple GFR estimation methods to achieve a comprehensive assessment of renal function, especially in rural populations with diverse demographic characteristics. The agreement between different equations suggests that clinicians can use either serum creatinine or cystatin C-based equations depending on the clinical context and available resources. The Kidney Disease Improving Global Outcomes (KDIGO) 2012 CKD Guideline recommends initial testing using serum creatinine

and a GFR estimating equation, followed by confirmatory testing with additional tests such as serum cystatin C or a clearance measurement in specific circumstances where eGFRcr is less accurate.[17] This study provides valuable insights into the assessment of renal function using different GFR estimation methods in a rural population. The results suggest that both creatinine and cystatin C-based equations are reliable for estimating GFR, with substantial agreement between the methods. Further research with larger and more diverse populations is recommended to validate these findings and explore the impact of regional and racial differences on renal function assessment.

CONCLUSION

The study found good agreement among various GFR estimation methods. The eGFR CKD-EPICr showed perfect agreement with the MDRD equation, while eGFR CKD-EPICys demonstrated substantial agreement with eGFR CKD-EPICr-Cys, suggesting their reliability in assessing renal function in rural populations.

Recommendation

Further population-based study with larger sample size is recommended

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